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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,558	03/19/2004	Rosa Cuberes Altisen	785-011731-US (PAR)	7436

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EXAMINER	
FREISTEIN, ANDREW B	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 07/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/804,558	CUBERES ALTISEN ET AL.	
	Examiner	Art Unit	
	Andrew B. Freistein	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *17,18 and 20-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,19 and 30-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and remarks filed 6/7/2006 have been entered. Claims 1-62 are currently pending in the instant application.

Restriction Requirement

Newly added claims 31-62 are drawn to compounds of formula (I) and are joined as part of Group I.

Pending Claim Rejections - 35 USC § 102

(1) Claims 1-6, 15, 19 & 30 were rejected under 35 U.S.C. 102(b) as being anticipated by Frigola et al, "7-Azetidinylquinolones as Antibacterial Agents. 3. Synthesis, Properties and Structure-Activity Relationships of the Stereoisomers Containing a 7-(3-Amino-2-methyl-1-azetidinyl) Moiety," J. Med. Chem. 38(7) 1203-15 (1995). As a result of the amendment filed 6/7/2006, which provides that R^1 must be at least mono-substituted phenyl, this rejection is withdrawn.

(2) Claims 1-6, 15, 19 & 30 were rejected under 35 U.S.C. 102(b) as being anticipated by Frigola et al., "7-Azetidinylquinolones as Antibacterial Agents. 2. Synthesis and Biological Activity of 7-(2,3-Disubstituted-1-azetidinyl)-4-oxoquinoline- and -1,8-naphthyridine-3-carboxylic Acids. Properties and Structure-Activity Relationships of Quinolones with an Azetidine Moiety," J. Med. Chem., 37(24), pp. 4195-4210 (1994). As a result of the amendment filed 6/7/2006, which provides that R^1 must be at least mono-substituted phenyl, this rejection is withdrawn.

(3) Claims 1-6 and 15 were rejected under 35 U.S.C. 102(b) as being anticipated by Pinol et al., US Pat. No. 5,073,646. As a result of the amendment filed

6/7/2006, which provides that R^1 must be at least mono-substituted phenyl, this rejection is withdrawn.

Pending Claim Rejections - 35 USC § 103

Claims 1-6, 15, 19 and 30 were rejected under 35 U.S.C. 103(a) as being unpatentable over Frigola et al., "7-Azetidinylquinolones as Antibacterial Agents. 2. Synthesis and Biological Activity of 7-(2,3-Disubstituted-1-azetidinyl)-4-oxoquinoline- and -1,8-naphthyridine-3-carboxylic Acids. Properties and Structure-Activity Relationships of Quinolones with an Azetidine Moiety," J. Med. Chem., 37(24), pp. 4195-4210 (1994). As a result of the amendment filed 6/7/2006, which provides that R^1 must be at least mono-substituted phenyl, this particular rejection is withdrawn. *Nevertheless, claims 1-6, 10-14, 19, 30, 31 and 33-61 are further rejected under 35 U.S.C. 103(a) as being unpatentable over Frigola et al. (see below).*

New Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16, 19 and 30-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(1) In claim 1, R^1 is defined to be "an at least mono-substituted phenyl group." However, last paragraph of claim 1 states, "with the proviso that compounds of formula I, in which R^1 and R^2 each represent an unsubstituted phenyl group, R^5 represents an $O\text{-}SO_2\text{-}R^6$ moiety and R^6 represents a methyl group are excluded."

The amendment to R^1 is an attempt to show novelty over the cited prior art, but because the substituents on the R^1 phenyl group are not provided in claim 1, Applicant fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Additionally, claim 31 is drawn to "compounds according to claim 2, where R^1 represents a phenyl group, which is **optionally** substituted by one or more substituents independently selected by one or more substitutents independently selected from the group consisting of..." (emphasis added). Although claim 31 depends on claim 2, which deleted "optionally," the claims are inconsistent.

In order to overcome this rejection, Applicant must specifically define the substituents on the phenyl group of R^1 and delete "optionally" in claim 31.

(2) Claims 1-16, 19 and 30-62 are rejected under 35 U.S.C. 112, second paragraph, for the definitions of R^9, R^{10}, R^{11}, R^{12} and R^{13}. In claim 1, R^5 was amended to delete the definitions "$NR^9SO_2R^{10}$ moiety or an O-CO-R^{11} moiety." However, claim 1 still has definitions for the variables R^9, R^{10}, R^{11}, R^{12} and R^{13} and it is unclear what these variables are intended to define. Additionally, claims 10-14, 42 and 48-61 further define compounds of formula I by specifically defining variables R^9, R^{10}, R^{11}, R^{12} and R^{13}. In order to overcome this rejection, these definitions must be deleted in claim 1 and claims 10-14 and 48-61 should be cancelled.

(3) Claims 1-16, 19 and 30-62 are rejected under 35 U.S.C. 112, second paragraph, because claim 1 is drawn to, "Substituted Azetidine compounds of formula I..." However, it is unclear what part of formula (I) is "substituted" and what the

substituents are. In order to overcome this rejection, "substituted" should be deleted from the beginning of claim 1.

New Claim Rejections - 35 USC § 103

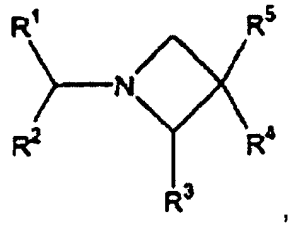
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

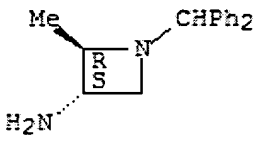
Claims 1-6, 10-14, 19, 30, 31 and 33-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frigola et al., "7-Azetidinylquinolones as Antibacterial Agents. 2. Synthesis and Biological Activity of 7-(2,3-Disubstituted-1-azetidinyl)-4-oxoquinoline- and -1,8-naphthyridine-3-carboxylic Acids. Properties and Structure-Activity Relationships of Quinolones with an Azetidine Moiety," J. Med. Chem., 37(24), pp. 4195-210 (1994).

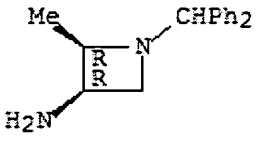
Claims 1-6, 10-14, 19 and 30 of the instant application are drawn to a compound of formula (I),  , wherein R^1 is at least mono-substituted phenyl; R^2 is phenyl; R^3 is an aliphatic group; R^4 is H; R^5 is an NH_2 moiety; R^8 is an optionally substituted 6-membered aryl group; with the exclusion of compounds wherein R^1 and R^2 are each unsubstituted phenyl, R^5 is $O\text{-}SO_2\text{-}R^6$ and R^6 is methyl.

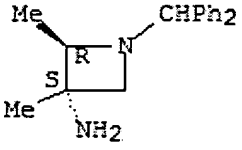
Claims 19 and 30 are drawn to a medicament comprising a compound of formula (I) and a pharmaceutically acceptable carrier.

Determining the Scope and Content of the Prior Art

Frigola et al. disclose the compounds:



, 

and 

(see p. 4196, Table 1, compounds 18f, 18g and 18j).

The compounds disclosed are used for antibacterial use and pharmacokinetic use (p. 4196, col. 1).

Ascertaining the Differences Between the Prior Art and the Instant Application

The instant application provides that "R^1 represents an at least mono-substituted phenyl group. Although no specific substituent is listed in claim 1, the Specification states that preferred substituents on R^1 are $C_{1\text{-}6}$alkyl (see p. 11). Therefore, the difference between the prior art and the instant application is that the prior art discloses

unsubstituted phenyl groups in position R1 and the instant application claims at least a mono-substituted phenyl group, wherein the substituent is C_1alkyl. Consequently, the difference between the prior art and the instant application is a Hydrogen atom versus a CH_3 group as the substituent on variable R^1.

Finding Prima Facie Obviousness

It is well established that the substitution of methyl for Hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. *In re Wood*, 199 USPQ 137 (CCPA 1978) and *In re Lohr*, 137 USPQ 548, 549 (CCPA 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

NO CLAIM IS ALLOWED.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Andrew B. Freistein
Patent Examiner, AU 1626

for

Joseph K. McKane
Supervisory Patent Examiner, AU 1626
Date: June 26, 2006